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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LEFFERS JR, GERALD G	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 09/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/675,525	BARRETT ET AL.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38 and 40-127* is/are pending in the application.

4a) Of the above claim(s) *4,10,13-21,43,51-53 and 55-126* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9,11,12,22-38,40-42,44-50,54 and 127* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a response, filed 6/28/2004, in which claim 1 was amended, claim 39 was cancelled and in which new claim 127 was added. Claims 1-38 and 40-127 are pending in the instant application, with claims 4, 10, 13-21, 43, 51-53 & 55-126 withdrawn from consideration as being directed to nonelected inventions. Claims 1-3, 5-9, 11-12, 22-38, 40-42, 44-50, 54 & 127 are under consideration in the instant application.

Response to Amendment

Any rejection of record not addressed herein is withdrawn. The newly presented grounds of rejection based on obviousness-type double patenting will not preclude the finality of this office action. Indeed, these grounds of rejection involve conflicting claims in a copending application newly discovered by the examiner, which has inventors in common with the instant application, and applicants did not call the attention of the Office to this application. Applicants will not be permitted to extend the prosecution of the present application by reason of their inaction with regard to notice to the Office of conflicting claims in a copending application, the discovery of which necessitated the new grounds of rejection at this advanced state of prosecution. Indeed, with appropriate notice, these grounds of rejection clearly could have been incorporated in a prior office action. This situation is clearly analogous to the policy of making an action final where applicants' material amendments to the claims necessitated a new ground of rejection, since in both instances it is the applicant who caused the rejection to be applied after the case had received an action on the merits. See M.P.E.P. § 706.07(a). The remaining new

grounds of rejection made in the instant action were necessitated by applicants' amendment of the claims in the response filed 6/28/2004 and this action is therefore FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-3, 5-9, 11-12, 22-38, 40-42, 44 & 127 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections, each of which was necessitated by applicants' amendment of the claims in the response filed 6/28/2004.**

Claims 1 and 127 are vague and indefinite in that the metes and bounds of the phrase "heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound" are unclear. The phrase is unclear in that the specification does not provide an explicit and limiting definition for what is meant by "decoding" the heterologous nucleic acid "tag" such that a particular structural/functional limitation is conveyed to the skilled artisan concerning the nucleic acid tag and in what manner the tag can be "decoded". For example, the specification teaches, "In some methods, the replicable genetic packages bear nucleic acid tags which serve to record at least one characteristic of a compound or pool of compounds attached to a clonal isolate of the package. *Usually* such a tag is a nucleic acid segment other than a segment that encodes for a peptide (or portion thereof) displayed by the replicable genetic package." (examiner's emphasis added; see page 16, lines 25-29 of the instant specification). The specification further teaches that one can use a library of such tags along with a "correspondence

regime" to identify the particular compound attached to the replicable genetic package (e.g. page 39, part VI). It is unclear, for example, in the absence of such a "correspondence regime" between the recited nucleic acid and the recited compound, what would necessarily be the sequence/structure of such a tag for a given compound.

Claims 40-42 & 44 are vague and indefinite in that they are now dependent upon a cancelled claim, claim 39.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejected claims are directed to a replicable genetic package, or a collection or such replicable genetic packages, displaying a compound other than a polypeptide expressed by the replicable genetic package wherein the replicable genetic package comprises a heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound. As indicated above, the metes and bounds of the phrase "heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound" are unclear. In the absence of a clear structural/functional characteristic conveyed by the phrase "a heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound", the phrase can be interpreted broadly. For example, the phrase can be reasonably interpreted as encompassing an embodiment

wherein a phage display particle comprises a nucleic acid encoding a given polypeptide operatively linked to a phage coat protein such that the fusion protein comprising the given polypeptide is displayed on the surface of the phage and wherein the phage particle further "displays" a compound bound to the fusion protein (e.g. an antibody that binds the given polypeptide or a small molecule substrate for an enzyme displayed on the phage). In such an example the nucleic acid encoding the desired polypeptide can be considered the nucleic acid tag that is "decoded" in the sense that the primary sequence of the given polypeptide can be determined from the nucleic acid sequence and a "characteristic" of the compound determined by the fact that it binds that particular, given polypeptide (e.g. the antibody binds a protein having the particular amino acid sequence encoded by the "tag"). In such an example, the fusion protein would serve as a "linker" or "package linker" for the displayed compound. With regard to claim 127, the term "collection" is interpreted broadly to encompass a teaching of multiple, different phage display particles displaying different polypeptides on their surface that bind different "compounds", without any particular limitation as to their proximity to one another (e.g. a mixture or pool of such replicable genetic packages).

Claims 1-3, 5-9, 11-12, 22, 35-37, 45-49, 54 & 127 are rejected under 35 U.S.C. 102(b) as being anticipated by Studier et al (U.S. Patent No. 5,766,905 A; see the entire patent). **This is a new rejection necessitated by applicants' amendment of the claims in the response filed 6/28/2004.**

Studier et al teach a bacteriophage T7-based phage display system for displaying fusion proteins on the surface of the T7 phage capsid (e.g. as fusion proteins comprising the desired

peptide sequence and p10B, the major capsid protein for T7; see the Abstract or column 3, top paragraph). Studier et al teach examples where DNA encoding substantially similar fragments for a given protein can be cloned into the display vector and binding techniques can be employed to identify subtle differences in binding affinity for a given target and/or to identify peptides that bind a variety of targets (e.g. proteases, receptors, antibodies and DNA), or alternatively, to identify proteins with altered enzymatic characteristics (e.g. column 5, lines 20-40). For example, the patent exemplifies embodiments where enzymatic activities were measured for different enzymes displayed on the surface of recombinant T7 phage (e.g. T7 endonuclease or B-galactosidase; e.g. see columns 17-18). Such displayed enzymes would necessarily have displayed on their surface for at least some time a small molecule compound (e.g. the B-galactosidase substrate) attached via binding to the displayed enzyme. The "collection" of PD2 phage that display T7 endonuclease which temporarily bind and cleave the different nucleic acids used as substrates in the endonuclease assay would necessarily meet the limitation of being a "collection" of different replicable genetic packages that display different compounds on their surface (i.e. the different M13 DNA fragments cleaved by the endonuclease; e.g. columns 17-18).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-6, 9, 11-12, 22, 26-33, 35-36, 44-50, 54 & 127 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 21-22, 30 & 32 of U.S. Patent No. 6,777,239 (see the entire patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. **This is a new rejection.**

The rejected claims are directed to a replicable genetic package, or a collection or such replicable genetic packages, displaying a compound other than a polypeptide expressed by the replicable genetic package wherein the replicable genetic package comprises a heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound. As indicated above, the metes and bounds of the phrase "heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound" are unclear. In the absence of a clear structural/functional characteristic conveyed by the phrase "a heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound", the phrase can be interpreted broadly. For example, the phrase can be reasonably interpreted as encompassing an embodiment wherein a phage display particle comprises a nucleic acid encoding a given polypeptide operatively linked to a phage coat protein such that the fusion protein comprising the given polypeptide is displayed on the surface of the phage and wherein the phage particle further "displays" a compound bound to the fusion protein (e.g. an antibody that binds the given

polypeptide or a small molecule substrate for an enzyme displayed on the phage). In such an example the nucleic acid encoding the desired polypeptide can be considered the nucleic acid tag that is "decoded" in the sense that the primary sequence of the given polypeptide can be determined from the nucleic acid sequence and a "characteristic" of the compound determined by the fact that it binds that particular, given polypeptide (e.g. the antibody binds a protein having the particular amino acid sequence encoded by the "tag"). In such an example, the fusion protein would serve as a "linker" or "package linker" for the displayed compound. With regard to claim 127, the term "collection" is interpreted broadly to encompass a teaching of multiple, different phage display particles displaying different polypeptides on their surface that bind different "compounds", without any particular limitation as to their proximity to one another (e.g. a mixture or pool of such replicable genetic packages).

The claims of the '239 patent are directed to a method of analyzing an amino acid sequence of polypeptides by determining whether they share an epitope, the method comprising: (a) providing a population of replicable genetic package/antibody reagents, each replicable genetic package/antibody reagent (package/antibody reagent) comprising (i) a replicable genetic package having a heterologous nucleic acid segment that encodes a first polypeptide displayed on the replicable genetic package and (ii) a captured antibody having a plurality of binding sites, each site having specific affinity for the first polypeptide, with at least one of the sites available for binding, the first polypeptide and the captured antibody complexed with it varying between at least some of the package/antibody reagents; (b) contacting the population of package/antibody reagents with a second polypeptide, whereby package/antibody reagents bearing captured antibodies having specific affinity for the second polypeptide bind to the second polypeptide; (c)

identifying at least one package/antibody reagent that binds to the second polypeptide; and (d) determining the nucleotide sequence of the nucleic acid segment of the at least one package/antibody reagent, whereby the amino acid sequence corresponding to the nucleotide sequence can be deduced and is an indication of the amino acid sequence of an epitope shared by the first and second polypeptide (e.g. Claim 1, Figures 1 and 15). In this example, the fusion polypeptide that binds the antibody clearly is encoded by a nucleic acid "tag" that is decoded to determine a characteristic of the compound (i.e. the second polypeptide) that is displayed on the surface of the replicable genetic package (i.e. the bound second protein comprises an epitope the same or similar to one on the fusion protein). Further, the replicable genetic packages comprise multiple, different package/antibody combinations that reasonably can be expected to display different compounds depending on the peptides with which the antibody interacts. The replicable genetic package can be a virus, bacteriophage, bacterial cell or spore, or a polysome. At least some of the plurality of different capture antibodies displayed on the surface of some of the replicable genetic packages have different sequences and bind to different epitopes (i.e. display separate peptide compounds that bind the capture antibody).

The claims of the '239 patent are very particular species claims that utilize replicable genetic packages, or collections thereof, that anticipate and necessarily make obvious the instant claims which are much more broadly directed to replicable genetic packages where the nature of the nucleic acid "tag" is not as defined, the use of a capture antibody is not required and where the displayed compound is not necessarily a peptide having a similar or identical epitope to one displayed on the replicable genetic package. With regard to the elected species, one of skill in the art, in order to identify which species provided support for the broad term "replicable genetic

package" in the recited methods would necessarily have referred to the teachings of the '239 specification, where phage T7 is an exemplified embodiment. Finally, the instant rejection is necessary in order to avoid possible harassment by multiple assignees having rights to the invention recited by the '239 claims, which would be improper.

Examiner's Note

Amendment of the base claims (i.e. claims 1, 45 and 127) to include the limitation of pending claim 34 (i.e. "wherein the heterologous nucleic acid tag is a nucleic acid segment other than a segment that encodes for a polypeptide displayed on the replicable genetic package") would obviate the prior art rejection and the obviousness-type double patenting rejection. It is not clear at this point whether such an amendment would sufficiently define what is intended by the phrase "heterologous nucleic acid tag that can be decoded to identify a characteristic of the compound" to overcome the rejection made above under 35 U.S.C. 112 2nd paragraph. Applicants' representative is invited to telephone the examiner in order to discuss possible language to overcome each of these grounds of rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

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